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AMENDMENTS TO THE CLAIMS

Please replace all prior versions and listings of claims with the amended claims as follows:

1-46. (Canceled)

47. (Currently amended) A composition comprising an effective amount of <u>a</u> compound of <u>claim 1 formula I:</u>

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or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, adjuvant, or vehicle, wherein:

 R^{1} is $-(L)_{m}R$, $-(L)_{m}Ar^{1}$, or $-(L)_{m}Cy^{1}$;

L is -S-, -O-, -N(R)-, or a C_{1-6} alkylidene chain wherein up to two non-adjacent methylene units of L are optionally and independently replaced by -S-, -O-, -N(R)-, -N(R)C(O)-, -N(R)C(S)-, -N(R)C(O)N(R)-, -N(R)C(S)N(R)-, -N(R)CO₂-, -C(O)-, -CO₂-, -C(O)N(R)-, -C(S)N(R)-, -OC(O)N(R)-, -SO₂-, -SO₂N(R)-, -N(R)SO₂-, -N(R)SO₂N(R)-, -C(R)=NN(R)-, -C(R)=N-O(R)-, -C(O)C(O)-, or -C(O)CH₂C(O)-;

m is 0 or 1;

- Ar¹ is an optionally substituted 5-7 membered monocyclic ring or an 8-10 membered bicyclic ring having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur;
- Cyl is an optionally substituted 3-7 membered saturated or partially unsaturated monocyclic ring having 0-3 heteroatems independently selected from nitrogen.

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oxygen, or sulfur, or an 8-10 membered saturated or partially unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein;

Ar¹ and Cy¹ are each optionally substituted with up to 5 occurrences of Z-R^X; wherein

each occurrence of Z is independently a bond or a C₁₋₆ alkylidene chain, wherein up to two non-adjacent methylene units of Z are optionally

replaced by -S-, -O-, -N(R)-, -N(R)C(O)-, -N(R)C(S)-, -N(R)C(O)N(R)-,

-N(R)C(S)N(R)-, $-N(R)C(O_2$ -, -C(O)-, $-CO_2$ -, -C(O)N(R)-, -C(S)N(R)-,

-OC(O)N(R)-, $-SO_2$ -, $-SO_2$ N(R)-, $-N(R)SO_2$ -, $-N(R)SO_2$ N(R)-,

-C(R)=NN(R)-, -C(R)=N-O(R)-, -C(O)C(O)-, or $-C(O)CH_2C(O)$ -;

each occurrence of RX is independently selected from -R', halogen, NO2, CN,

-OR', -SR', $-N(R')_2$, -N(R')C(O)R', -N(R')C(S)R', $-N(R')C(O)N(R')_2$,

 $-N(R')C(S)N(R')_2$, $-N(R')CO_2R'$, -C(O)R', -C(S)R', $-CO_2R'$, -OC(O)R',

 $-C(O)N(R')_2$, $-C(S)N(R')_2$, $-OC(O)N(R')_2$, -S(O)R', $-SO_2R'$, $-S(O)_2R'$;

 $-SO_2N(R')_2$, $-N(R')SO_2R'$, $-N(R')SO_2N(R')_2$, -C(O)C(O)R',

 $-C(O)CH_2C(O)R'$, -NR'NR'C(O)R', $-NR'NR'C(O)N(R')_2$, -

 $NR'NR'CO_2R'$, -C(O)N(C)R') R', -C(NOR') R', $-S(O)_3R$, -N(OR')R',

-C(=NH)-N(R')₂; or -(CH₂)₀₋₂NHC(O)R'; wherein

each occurrence of R is independently hydrogen or an optionally substituted

C₁₋₆ aliphatic group,

each occurrence of R' is independently hydrogen or an optionally substituted

C₁₋₆ aliphatic group, an optionally substituted C₆₋₁₀ aryl ring, an optionally substituted heteroaryl ring having 5-10 ring atoms, or an optionally substituted heterocyclyl ring having 3-10 ring atoms; or

R and R' or two occurrences of either R or R' are taken together with the atoms to which they are bound to form an optionally

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substituted 5-8 membered saturated, partially unsaturated, or aryl ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur; or

two occurrences of either R' or R on the same nitrogen are taken

together with the nitrogen atom to which they are bound to form an
optionally substituted 5-8 membered saturated, partially
unsaturated, or aryl ring having 1-4 heteroatoms independently
selected from nitrogen, oxygen, or sulfur;

R² is hydrogen, CN, -SR, -OR, -CO₂R, -OC(O)R, -C(O)R, -C(O)N(R)₂, -N(R)₂, -N(R)C(O)R, or an optionally substituted C_{1-6} aliphatic group;

T is CR³;

each of A¹, A², and A³ is, independently, CR⁴;

- R^3 is selected from hydrogen, halogen, NO_2 , CN, -SR, -OR, $-N(R)_2$, or an optionally substituted C_{1-6} aliphatic group; and
- R⁴ is selected from halogen, NO₂, CN, -(L)_mR, -(L)_mAr¹, or -(L)_mCy¹; or

 two R⁴ groups on adjacent atoms are taken together to form an optionally
 substituted 5-7 membered partially unsaturated or fully unsaturated ring
 having 0-3 heteroatoms independently selected from oxygen, sulfur, or
 nitrogen, wherein;

each ring formed by two R^4 groups on adjacent atoms taken together is optionally substituted with up to 4 occurrences of $Z \cdot R^X$.

- 48. (Canceled)
- 49. (Original) The composition of claim 47, additionally comprising a therapeutic agent selected from a chemotherapeutic or anti-proliferative agent, an anti-inflammatory agent, an immunomodulatory or immuno suppressive agent, a neurotrophic factor, an

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agent for treating cardiovascular disease, an agent for treating destructive bone disorders, an agent for treating liver disease, an anti-viral agent, an agent for treating blood disorders, an agent for treating diabetes, or an agent for treating immunodeficiency disorders.

50. (Currently amended) A method of inhibiting CDK-2, cMET, FLT-3, JAK-3, GSK-3, IRAK-4, SYK, p70S6K, TAK-1, or ZAP-70 kinase activity in[[:]]

(a) a patient; or

(b) a biological sample, wherein said biological sample is selected from a cell culture, biopsied material obtained from a mammal, saliva, urine, feces, semen, or tears, or an extract thereof; which method comprises administering to said patient, or contacting said biological sample with a composition according to claim 47 or [[:]] a compound of formula I:

]

or a pharmaceutically acceptable salt thereof, wherein:

 R^{l} is -(L)_mR, -(L)_mAr^l, or -(L)_mCy^l;

L is -S-, -O-, -N(R)-, or a C₁₋₆ alkylidene chain wherein up to two non-adjacent methylene units of L are optionally and independently replaced by -S-, -O-, -N(R)-, -N(R)C(O)-, -N(R)C(S)-, -N(R)C(O)N(R)-, -N(R)C(S)N(R)-, -N(R)CO₂-, -C(O)-, -CO₂-, -C(O)N(R)-, -C(S)N(R)-, -OC(O)N(F:)-, -SO₂-, -SO₂N(R)-, -N(R)SO₂-, -N(R)SO₂N(R)-, -C(R)=NN(R)-, -C(R)=N-O(R)-, -C(O)C(O)-, or -C(O)CH₂C(O)-; m is 0 or 1;

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Ar¹ is an optionally substituted 5-7 membered monocyclic ring or an 8-10 membered bicyclic ring having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

Cy¹ is an optionally substituted 3-7 membered saturated or partially unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-10 membered saturated or partially unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein;

Ar¹ and Cy¹ are each optionally substituted with up to 5 occurrences of Z-R^X; wherein

each occurrence of Z is independently a bond or a C₁₋₆ alkylidene chain, wherein up to two non-ad acent methylene units of Z are optionally replaced by -S-, -O-, -N(R)-, -N(R)C(O)-, -N(R)C(S)-, -N(R)C(O)N(R)-, -N(R)C(S)N(R)-, -N(R)C(O)-, -C(O)-, -C(O)N(R)-, -C(S)N(R)-, -OC(O)N(R)-, -SO₂-, -SO₂N(R)-, -N(R)SO₂-, -N(R)SO₂N(R)-, -C(R)=NN(R)-, -C(R)=N-O(R)-, -C(O)C(O)-, or -C(O)CH₂C(O)-;

each occurrence of R^X is independently selected from -R', halogen, NO₂, CN, -OR', -SR', -N(R')₂, -N(R')C(O)R', -N(R')C(S)R', -N(R')C(O)N(R')₂,

 $-N(R')C(S)N(R')_2$, $-N(R')CO_2R'$, -C(O)R', -C(S)R', $-CO_2R'$, -OC(O)R',

 $-C(O)N(R')_2$, $-C(S)N(R')_2$, $-OC(O)N(R')_2$, -S(O)R', $-SO_2R'$, $-S(O)_3R'$;

 $-SO_2N(R')_2$, $-N(R')SO_2R'$, $-N(R')SO_2N(R')_2$, -C(O)C(O)R',

-C(O)CH2C(O)R', -NR'NR'C(O)R', -NR'NR'C(O)N(R')2, -

 $NR'NR'CO_2R'$, -C(O)N(OR')R', -C(NOR')R', $-S(O)_3R$, -N(OR')R',

-C(=NH)-N(R')2; or -(CH2)0-2NHC(O)R'; wherein

each occurrence of R is independently hydrogen or an optionally substituted

C₁₋₆ aliphatic group,

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each occurrence of R' is independently hydrogen or an optionally substituted

C₁₋₆ aliphatic group, an optionally substituted C₆₋₁₀ aryl ring, an optionally substituted heteroaryl ring having 5-10 ring atoms, or an optionally substituted heterocyclyl ring having 3-10 ring atoms; or

R and R' or two occurrences of either R or R' are taken together with
the atoms to which they are bound to form an optionally
substituted 5-8 membered saturated, partially unsaturated, or aryl
ring having 0-4 heteroatoms independently selected from nitrogen,
oxygen, or sulfur; or

two occurrences of either R' or R on the same nitrogen are taken
together with the nitrogen atom to which they are bound to form an
optionally substituted 5-8 membered saturated, partially
unsaturated, or aryl ring having 1-4 heteroatoms independently
selected from nitrogen, oxygen, or sulfur;

R² is hydrogen, CN, -SR, -OR, -CO₂R, -OC(O)R, -C(O)R, -C(O)N(R)₂, -N(R)₂, -N(R)C(O)R, or an optionally substituted C_{1-6} aliphatic group;

T is CR³;

each of A¹, A², and A³ is, independently, CR⁴;

 R^3 is selected from hydrogen, halogen, NO_2 , CN, -SR, -OR, $-N(R)_2$, or an optionally substituted C_{1-6} aliphatic group; and

R⁴ is selected from halogen, NO₂, CN, -(L)_mR, -(L)_mAr¹, or -(L)_mCy¹; or

two R⁴ groups on adjacent atoms are taken together to form an optionally
substituted 5-7 membered partially unsaturated or fully unsaturated ring
having 0-3 heteroatoms independently selected from oxygen, sulfur, or
nitrogen, wherein;

each ring formed by two R⁴ groups on adjacent atoms taken together is optionally substituted with up to 4 occurrences of Z-R^X

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a) a composition of claim 47; or

b) a compound of claim 1.

- 51. (Currently amended) The method of claim 50, wherein the method comprises inhibiting CDK-2, cMET[[,]] FLT-3, JAK-3, GSK-3, IRAK-4, SYK, p70S6K, TAK-1, or ZAP-70 activity.
- 52. (Currently amended) A method of treating or lessening the severity of a disease or [[of]] condition selected from cancer[[,]] or a proliferative disorder, a cardiac disorder, a neurodegenerative disorder, an autoimmune disorder, a condition associated with organ transplant, an inflammatory disorder, an immunologically mediated disorder, a viral disease, or a bone disorder, comprising the step of administering to said patient[[:]]

[[a)]] a composition of claim 47; 3r

b) a compound of claim 1.

53. (Original) The method according to claim 52, comprising the additional step of administering to said patient an additional therapeutic agent selected from a chemotherapeutic or anti-proliferative agent, an anti-inflammatory agent, an immunomodulatory or immunosuppressive agent, a neurotrophic factor, an agent for treating cardiovascular disease, an agent for treating destructive bone disorders, an agent for treating liver disease, an anti-viral agent, an agent for treating blood disorders, an agent for treating diabetes, or an agent for treating immunodeficiency disorders, wherein:

said additional therapeutic agent is appropriate for the disease being treated; and said additional therapeutic agent is administered together with said composition as a single dosage form or separately from said composition as part of a multiple dosage form.

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(Currently amended) The method according to claim 52, wherein said disease is 54. cancer, Alzheimer's disease, restenosis, angiogenesis, glomerulonephritis, eytomegalovirus, HIV, herpes virus, varicella zoster virus, human cytomegalovirus, psoriasis, atherosclerosis, inflammatory bowel disease, sepsis, alopecia, rheumatoid arthritis, diabetes, manie depressive disorder neurodegenerative and neurological diseases, cardiomyocyte hypertrophy, aut simmune diseases, inflammatory diseases, metabolic diseases, cardiovascular diseases, diabetes, Huntington's disease, Parkinson's disease, AIDS associated dementia, multiple selerosis (MS), sehizophrenia, reperfusion/ischemia, stroke, baldness, acute-myelogenous leukemia (AML, Lou Gehrig's disease), acute lymphocytic leukemia (Al.L.), or mastocytosis and gastrointestinal stromal tumor (GIST), hematopoietic disorders, in particular, acute promyelocytic leukemia (APL), osteoporosis, hepatitis B virus, proliferative and hyperproliferative diseases, immunologically-mediated diseases including rejection of transplanted organs or tissues and Acquired Immunodeficiency Syndrome (AIDS), reversible obstructive airways diseases including asthma, such as bronchial, allergie, intrinsic, extrinsic and dust asthma, particularly chronic or inveterate asthma-(e.g. late asthma airways hyper-responsiveness) and bronchitis, those conditions characterised by inflammation of the nusal mucus membrane, including acute rhinitis, allergic, atrophic thinitis and chronic rhinitis including rhinitis cascosa, hypertrophic rhinitis, rhinitis purulenta, rhinitis sicca and rhinitis medicamentosa; membranous rhinitis including croupous, fibrinous and pseudomembranous rhinitis and scrofoulous rhinitis, seasonal rhinitis including rhinitis nervosa (hay fever) and vasomotor rhinitis, sarcoidosis, farmer's lung and related diseases, fibroid-lung, and idiopathic interstitial pneumonia.

55. (Canceled)

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56. (Currently amended) The method according to claim <u>52</u> [[55]], wherein said <u>disease eancer</u> is selected from renal <u>cancer</u>, colon <u>cancer</u>, breast <u>cancer</u>, prostate <u>cancer</u>, hepatic <u>cancer</u>, pancreatic <u>cancer</u>, ovarian <u>cancer</u>, [[or]] lung cancer, or certain B-cell leukemias or lymphomas.

57-58. (Canceled)

59. (New) The composition according to claim 47, wherein R^1 is $-(L)_m A r^1$ and $A r^1$ is selected from one of the following groups:

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60. (New) The composition according to claim 59, wherein Ar¹ is selected from one of the following groups:

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61. (New) The composition according to claim 59, wherein R^1 is $-(L)_m$ -Ar¹, m is 1 and compounds have the formula IA-1:

62. (New) The composition according to claim 59, wherein Ar¹ is phenyl with 0-5 occurrences of ZR^X and compounds have the formula IA-1-5:

63. (New) The composition according to claim 47, wherein R^1 is $-(L)_m$ -Cy¹ and compounds have the formula IA-2:

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64. (New) The composition according to claim 63, wherein Cy¹ is selected from one of the following groups:

- 65. (New) The composition according to claim 59, wherein L is an optionally substituted C₁₋₆ straight or branched alkylidene chain wherein one methylene unit of L is optionally replaced by O, NR, NRCO, NRCS, NRCONR, NRCSNR, NRCO₂, CO, CO₂, CONR, CSNR, OC(O)NR, SO₂, SO₂NR, NRSO₂, NRSO₂NR, C(O)C(O), or C(O)CH₂C(O).
- 66. (New) The composition according to claim 65, wherein L is an optionally substituted C₁₋₆ straight or branched alkylidene chain wherein one methylene unit of L is optionally replaced by O, NR, NRCO, CO, CONR, SO₂NR, NRSO₂.

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67. (New) The composition according to claim 47, wherein R¹ is -(L)_mR, L is an optionally substituted C₁₋₆ straight or branched alkylidene chain wherein one methylene unit of L is optionally replaced by O, NR, NRCO, NRCONR, NRCO₂, CO, CO₂, CONR, OC(O)NR, SO₂, SO₂NR, NRSO₂, NRSO₂NR, and R is an optionally substituted C₁₋₆ aliphatic group.

- 68. (New) The composition according to claim 47, wherein R^2 is hydrogen, -CN, -OR, -CO₂R, -OC(O)R, -C(O)R, -C(O)N(R)₂, -N(R)₂, -N(R)C(O)R, or an optionally substituted C_{1-6} aliphatic group.
- 69. (New) The composition according to claim 68, wherein \mathbb{R}^2 is hydrogen or an optionally substituted \mathbb{C}_{1-6} aliphatic group.
- 70. (New) The composition according to claim 69, wherein R² is hydrogen, methyl, ethyl, n-propyl, isopropyl, or cyclopropyl.
- 71. (New) The composition according to claim 47, wherein \mathbb{R}^2 is hydrogen and compounds have the formula \mathbf{B} :

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- 72. (New) The composition according to claim 47, wherein T is CR³ and R³ is hydrogen, halogen, CN, or an optionally substituted C₁₋₆ aliphatic group.
- 73. (New) The composition according to claim 72, wherein R³ is hydrogen, halogen, CF₃, methyl, ethyl, n-propyl, isopropyl, or cyclopropyl.
- 74. (New) The composition according to claim 47, wherein T is CR³, R³ is hydrogen and compounds have the formula IC:

IC.

- 75. (New) The composition according to claim 47, wherein A^1 is CR^4 and R^4 is halogen, CN, $-(L)_mR$, $-(L)_mAr^1$, or $-(L)_mCy^1$.
- 76. (New) The composition according to claim 75, wherein L is an optionally substituted C₁₋₆ straight or branched alky idene chain wherein one methylene unit of L is optionally replaced by O, NR, NRCO, NRCONR, NRCO₂, CO, CO₂, CONR, OC(O)NR, SO₂, SO₂NR, NRSO₂, NRSO₂NR, C(O)C(O), or C(O)CH₂C(O).
- 77. (New) The composition according to claim 75, wherein A¹ is CR⁴ and R⁴ is halogen, CN, or R.

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78. (New) The composition according to claim 75, wherein A^1 is CR^4 , R^4 is $-(L)_mR$, and compounds have the formula ID-1:

79. (New) The composition according to claim 75, wherein A¹ is CR⁴, R⁴ is -(L)_mAr¹, and compounds have the formula ID-2:

$$Ar_{\parallel}^{1} \qquad N(OH)$$

$$m(L) \qquad R^{2}$$

$$A^{2}_{A/3} \qquad O \qquad R^{1}$$

ID-2.

80. (New) The composition according to claim 75, wherein A^1 is CR^4 , R^4 is $-(L)_mCy^1$, and compounds have the formula ID-3:

$$Cy^{1} \qquad N(OH)$$

$$m(L) \qquad R^{2}$$

$$A^{2} \chi \qquad O \qquad R^{1}$$

$$D-3.$$

81. (New) The composition according to claim 47, wherein A^2 is CR^4 and R^4 is halogen, CN, $-(L)_mR$, $-(L)_mAr^1$, or $-(L)_mCy^1$.

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- 82. (New) The composition according to claim 81, wherein L is an optionally substituted C₁₋₆ straight or branched alkylidene chain wherein one methylene unit of L is optionally replaced by O, NR, NRCO, NRCONR, NRCO₂, CO, CO₂, CONR, OC(O)NR, SO₂, SO₂NR, NRSO₂, NRSO₂NR, C(O)C(O), or C(O)CH₂C(O).
- 83. (New) The composition according to claim 81, wherein A^2 is CR^4 and R^4 is halogen or R.
- 84. (New) The composition according to claim 81, wherein A^2 is CR^4 and R^4 is $-(L)_mR$, wherein L is -O- or -N(R)-.
- 85. (New) The composition according to claim 81, wherein A^2 is CR^4 , R^4 is $-(L)_mCy^1$, m is 0 and Cy^1 is 2-2, 2-5, 2-6, 2-7, 2-8, or 2-12.
- 86. (New) The composition according to claim 81, wherein A^2 is CR^4 , R^4 is $-(L)_mAr^1$, m is 0 and Ar^1 is 1-5, 1-6, 1-11, 1-12, 1-13, 1-19, 1-24, or 1-25.
- 87. (New) The composition according to claim 81, wherein A² is CR⁴, R⁴ is -(L)_mR, and compounds have the formula IE-1:

IE-1.

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88. (New) The composition according to claim 81, wherein A² is CR⁴, R⁴ is -(L)_mAr¹, and compounds have the formula IE-2:

IE-2.

89. (New) The composition according to claim 81, wherein A^2 is CR^4 , R^4 is $-(L)_mCy^1$, and compounds have the formula IE-3:

$$M(L)$$
 A^{1}
 A^{3}
 Cy^{1}
 A^{3}
 Cy^{1}
 A^{3}
 A^{3}
 Cy^{1}
 A^{3}
 $A^$

- 90. (New) The composition according to claim 47, wherein A^3 is CR^4 and R^4 is halogen, CN, $-(L)_mR$, $-(L)_mAr^1$, or $-(L)_mCy^1$.
- 91. (New) The composition according to claim 90, wherein L is an optionally substituted C₁₋₆ straight or branched alky idene chain wherein one methylene unit of L is optionally replaced by O, NR, NRCO, NRCONR, NRCO₂, CO, CO₂, CONR, OC(O)NR, SO₂, SO₂NR, NRSO₂, NRSO₂NR, C(O)C(O), or C(O)CH₂C(O).
- 92. (New) The composition according to claim 90, wherein A³ is CR⁴ and R⁴ is halogen or R.

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- 93. (New) The composition according to claim 90, wherein A^3 is CR^4 and R^4 is $-(L)_mR$, wherein L is -O- or -N(R)-.
- 94. (New) The composition according to claim 90, A^3 is CR^4 , R^4 is $-(L)_mCy^1$, m is 0 and Cy^1 is 2-2, 2-5, 2-6, 2-7, 2-8, or 2-12.
- 95. (New) The composition according to claim 90, wherein A^3 is CR^4 , R^4 is $-(L)_mAr^1$, m is 0 and Ar^1 is 1-5, 1-6, 1-11, 1-12, 1-13, 1-19, 1-24, or 1-25.
- 96. (New) The composition according to claim 90, wherein A³ is CR⁴, R⁴ is -(L)_mR, and compounds have the formula IF-1:

97. (New) The composition according to claim 90, wherein A³ is CR⁴, R⁴ is -(L)_mAr¹, and compounds have the formula IF-2:

IF-2.

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98. (New) The composition according to claim 90, wherein A^3 is CR^4 , R^4 is $-(L)_mCy^1$, and compounds have the formula IF-3:

99. (New) The composition according to claim 47, wherein T is CR³, A¹, A² and A³ are each CR⁴ and compounds have the formula IG-1:

$$R^4$$
 R^4 R^4 R^4 R^4 R^4 R^4 R^4 R^4

IG-1.

100. (New) The composition according to claim 47, wherein each ZR^X is independently halogen, NO₂, CN, or an optionally substituted group selected from C₁₋₄ alkyl, aryl, aralkyl, -N(R')₂, -CH₂N(R')₂, -OR', -CH₂OR', -SR', -CH₂SR', -COOR', or -S(O)₂N(R')₂.

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101. (New) The composition according to claim 47, selected from one of the following compounds:

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I-30

I-29

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